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UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE BOARD OF PATENT APPEALS
AND INTERFERENCES

Ex parte STUART L. SCHREIBER and GERALD R. CRABTREE

Appeal 2007-3483
Application 09/834,424
Technology Center 1600

Decided: September 29, 2008

Before TONI R. SCHEINER, DEMETRA J. MILLS, and ERIC GRIMES, *Administrative Patent Judges*.

MILLS, *Administrative Patent Judge*.

DECISION ON APPEAL

This is an appeal under 35 U.S.C. § 134. The Examiner has rejected the claims for lack of written description and obviousness. We have jurisdiction under 35 U.S.C. § 6(b).

The following claim is representative.

8. A method for preparing an agent that effects a biological event mediated by the association of two or more endogenous cell surface receptor molecules, the method comprising preparing an agent which includes a first

non-peptidic moiety that binds to one of the cell surface receptor molecules covalently linked to a second non-peptidic moiety that binds to the other cell surface receptor molecule, wherein the agent binds to both cell surface receptor molecules.

Cited References

Finn Wold, "Bifunctional Reagents", Methods in Enzymology, vol. 11 (1966), pp. 617-640.

Tae H. Ji, "Bifunctional Reagents", Methods in Enzymology, vol. 91 (1993), pp. 580-609.

Grounds of Rejection

1. Claims 8-29 stand rejected under 35 U.S.C. § 112, first paragraph as failing to comply with the written description requirement.

2. Claims 8-16 and 18-27 stand rejected under 35 U.S.C. § 102(b) as anticipated by Wold.

3. Claims 8-29 stand rejected under 35 U.S.C. § 102(b) as anticipated by Ji.

DISCUSSION

Background

"Dimerization and oligomerization of proteins are general biological control mechanisms that contribute to the activation of cell surface receptors, transcription factors, vesicle fusion proteins and other classes of intra- and extracellular proteins. The present inventors developed a general procedure for the regulated (inducible) dimerization or oligomerization of intracellular

proteins. This is accomplished using ligands, preferably '*small molecule*' ligands, which can bind to and cross-link two or more protein molecules endogenous to the cells, *i.e.,* proteins native to a cell or invading organism thereof. Such multivalent ligands which . . . promote the association of endogenous proteins in cells to effect a biological event have been referred to as 'chemical inducers of dimerization' (CIDs), or simply 'dimerizers'. (Spec. 3.)

"Many signaling pathways are triggered by the binding of extracellular ligands to cell surface receptors." (Spec. 1.) "In principle, any two target proteins can be induced to associate by treating the cells or organisms that harbor them with an appropriate dimerizer, preferably a cell permeant, synthetic dimerizer." (Spec. 3.)

Claim Interpretation

We recognize that during prosecution before the Office, claims are to be given their broadest reasonable interpretation consistent with the Specification as it would be interpreted by one of ordinary skill in the art. *In re American Academy of Science Tech Center*, 367 F.3d 1359, 1364 (Fed. Cir. 2004).

Appellants take the position that the term "binds" in the claims should be interpreted in view of the Specification. (Br. 20.) Appellants argue that "the specification makes it clear to the skilled person that the term 'binds' refers to non-covalent association. For example, on page 11, lines 13-18, the Specification introduces the 'dimerizing' agents by describing their binding properties in terms of binding affinities (Kd below about 10^{-6}, more

preferably below about 10^{-7}, 10^{-8} or 10^{-9})." (Br. 20.[1]) Appellants further argue that a "skilled person would appreciate that binding affinities are only used in reference to non-covalent associations, not covalent bonds." (Br. 20.) Appellants contend that the Specification's "discussion of *affinity* assays for identifying receptor binding moieties on pages 14-19 and the discussion of exemplary receptor binding moieties on page 13, lines 19-25 (all non-peptidic moieties that are known to bind non-covalently to proteins) further reinforces that the claim term 'binds' refers to non-covalent associations, not covalent bonds." (Br. 20.) Finally, Appellants note that "the specification and claims explicitly use the terms 'covalently linked', 'covalently joined' and 'covalently attached' to describe the covalent bond between the first and second non-peptidic moieties of the agent (e.g., see page 4, lines 25-28; page 13, lines 7-9 and 15-17; and claims 8 and 19)." (Br. 20.) Appellants conclude that a "skilled person would appreciate that this further differentiates the claim term 'binds' from covalent bonding." (Br. 20.)

The Examiner, on the other hand, argues that the term "binds" in the claims does not exclude covalent binding. (Ans. 14.)

We agree with Appellants that, when read in view of the Specification, the term "binding" refers to non-covalent association. This interpretation is supported by the claims language itself, which distinguishes between "binding" and "covalantly linked," as well as the passages in the

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[1] Throughout this Decision we refer to the Brief filed Oct. 2, 2006.

Specification cited by Appellants. This claim interpretation will control our decision below.

1. Claims 8-29 stand rejected under 35 U.S.C. § 112, first paragraph as failing to comply with the written description requirement.

The Examiner contends that claims 8 and 19 are "genus claims in terms of any methods of preparing any agent made up of two nonpeptidic moieties that has the ability to bind two cell surface receptors (claims 8-18) or two endogenous protein mediators (claims 19-29) in order to effect a biological event." (Ans. 4.)

While the Examiner acknowledges the Specification "specifically mentions several possible agents such as immunophilins (i.e. FK506 or rapamycin) and other ligands that bind to a receptor or binding partner, and further state[s] that 'other compounds capable of binding to those receptors or to other endogenous constituents may be readily identified using a variety of approaches' (page 14, lines 12-13 of the specification)," the Examiner argues that "[n]one of these moieties have been shown, when combined with a second non-peptidic moiety, to effect a biological event, and therefore it is unclear that these 'dimerizers' will serve to actually activate a signal transduction/biological event by dimerizing their targets." (Ans. 4.)

The Examiner argues that there is

> no description of even a single compound that is comprised of two non-peptidic moieties that each bind to a cell surface receptor, or endogenous protein mediator, where the agent can effect a biological event mediated by the association of the two receptors or endogenous protein mediators. … [T]he skilled artisan cannot envision a sufficient number of agents

> which include two non-peptide moieties that bind to cell surface receptors or endogenous protein mediators, wherein the compounds have the ability to effect a biological event mediated by the association of the two cell surface receptors or endogenous protein mediators. There is no description of a structural feature that correlates with the functional ability of an agent to bind two cell surface receptors, or two endogenous protein mediators in a manner which results in an effect on a biological event mediated by the association of said receptors or endogenous protein mediators. Irrespective of the fact that such disclosed agents as immunophilin-based agents are questionable with respect to their functionality in the claimed invention, there is not even a disclosure that the immunophilin-based agents are representative of all agents within the genus of compounds that are effective to bind to two receptors or endogenous protein mediators in a manner effective to elicit an effect on a biological event. As a result, the instant specification does not describe the method for preparing agents which effect a biological event in such a clear and concise manner so as to indicate that the appellant had possession of these agents at the time of filing of the application. Thus the written description requirement has not been satisfied.

(Ans. 4-5.)

Appellants contend that "[t]echnologies for identifying non-peptidic agents that bind to a given target were well established at the time the present application was filed. A variety of such agents were already known and available (see, for example, page 14 of the specification)." (Br. 12-13.)

Appellants further argue that

> the specification includes references to a variety of binding - agents (e.g., benzodiazepines, prostaglandins, beta-turn mimetics, alpha- and beta-blockers, etc. on page 14, lines 7-11 of the specification) that were available at the time the application was filed, and that were known to bind protein

> mediators of biological events. Collections of synthetic compounds and combinatorial libraries of compounds were also available (see page 19, lines 1-2 and Exhibits E-G). The specification also defines the characteristics and methods that could be used to test these and other agents for desirable binding ability (see, for example, pages 15-19). Thus, a huge number of useful agents were already known and available in the art; others could readily be identified as they came available. An oligomerizing agent for a protein mediator of interest could therefore be prepared by selecting a known binding agent or by screening available agents for binding against the protein mediator. No further guidance is required to describe possession of the invention.

(Br. 14.)

The Examiner "'bears the initial burden ... of presenting a prima facie case of unpatentability.' ... Insofar as the written description requirement is concerned, that burden is discharged by 'presenting evidence or reasons why persons skilled in the art would not recognize in the disclosure a description of the invention defined by the claims'" *In re Alton*, 76 F.3d 1168, 1175 (Fed. Cir. 1996). "[T]he written description requirement can be met by 'show[ing] that an invention is complete by disclosure of sufficiently detailed, relevant identifying characteristics ... i.e., complete or partial structure, other physical and/or chemical properties, functional characteristics when coupled with a known or disclosed correlation between function and structure, or some combination of such characteristics.'" *Enzo Biochem, Inc. v. Gen-Probe Inc.*, 323 F.3d 956, 964 (Fed. Cir. 2002) (emphasis omitted, bracketed material original).

The purpose of the written description requirement is to "ensure that the scope of the right to exclude, as set forth in the claims does not

overreach the scope of the inventor's contribution to the field as far as described in the patent specification." *Reiffin v. Microsoft Corp*, 214 F.3d 1342, 1345 (Fed. Cir. 2000). To that end, to satisfy the written description requirement, the inventor "must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the invention." *Vas-Cath Inc. v. Mahurkar*, 935 F.2d 1555, 1563-64 (Fed. Cir. 1991). We point out that it is not necessary for the specification to describe the claimed invention *ipsissimis verbis*; all that is required is that it reasonably convey to those skilled in the art that, as of the filing date sought, the inventor was in possession of the claimed invention. *Union Oil of California v. Atlantic Richfield Co.*, 208 F.3d 989, 997 (Fed. Cir. 2000); *Vas-Cath Inc. v. Mahurkar*, 935 F.2d at 1563- 64; *In re Gosteli*, 872 F.2d 1008, 1012 (Fed. Cir. 1989); *In re Edwards*, 568 F.2d 1349, 1351-52 (CCPA 1978).

It has been held that a claimed DNA could be described without, necessarily, disclosing its structure. *See Enzo Biochem, Inc. v. Gen-Probe Inc.*, 323 F.3d 956, 964 (Fed. Cir. 2002). Our appellate review court has also noted that "*Eli Lilly* did not hold that all functional descriptions of genetic material necessarily fail as a matter of law to meet the written description requirement; rather, the requirement may be satisfied if in the knowledge of the art the disclosed function is sufficiently correlated to a particular, known structure." *Amgen, Inc. v. Hoechst Marion Roussel, Inc.*, 314 F.3d 1313, 1332 (Fed. Cir. 2003).

Here, we agree with the Appellants that the Specification conveys with reasonable clarity to those skilled in the art that, as of the filing date

sought, they were in possession of the invention as claimed. In particular, the Specification provides that "binding compounds for use in the invention, may, but need not, bind to the mediator in a precise fashion required to inhibit, agonize or antagonize—they need only *bind* to the mediator." (Spec. 14.)

The Specification provides that dimerizers capable of binding to two or more protein molecules have the formula: linker—{rbm_1, rbm_2…rbm_n}, wherein in n is 2 or greater and rbm_1-rbm_n are receptor binding moieties (rbm). (Spec. 13 and 24-25.) The Specification exemplifies rbm moieties such as FK-506, cyclosporine-type moieties, rapamycin and steroids or tetracycline associated with linkers. (Spec. 13, and 24-25.) General methodology for assaying for additional rbms is set forth in the Specification at pages 15-18. Linker moieties are also exemplified in the Specification at pages 13 and 19-21. Further described is a method for finding the ability of a test substance (agent which includes a first non-peptidic moiety) to bind to selected receptors or block the receptor-mediated interaction in the presence of the receptor's ligand. (Spec. 16.)

The Specification also describes receptor structures and ligands for the receptors that are known in the art (Spec. 4, 8 (Table I)) and states that it is further known that signal transduction by cytokines and growth factors is accomplished by ligand-mediated receptor binding. (Spec. 8.) Finally, the Specification discloses that other signal transduction proteins such as tyrosine kinases which associate with receptors are also known in the art. (Spec. 9.)

The descriptive text needed to meet the written description requirement varies with

> the nature and scope of the invention at issue, and with the scientific and technologic knowledge already in existence. The law must be applied to each invention that enters the patent process, for each patented advance is novel in relation to the state of the science. Since the law is applied to each invention in view of the state of relevant knowledge, its application will vary with differences in the state of knowledge in the field and differences in the predictability of the science.

Capon v. Eshhar, 418 F.3d 1349, 1356-1357 (Fed. Cir. 2005). We do not find that the Examiner has given appropriate weight to the state of knowledge in the field of the invention, as outlined in the Specification. In addition, because the binding compounds for use in the invention need not bind to the mediator in a precise fashion (Spec. 14) we do not find that the Examiner has properly characterized the level of unpredictability in the art.

In summary, we find that, in view of the above, the Examiner has not adequately shown that the Specification does not convey with reasonable clarity to those skilled in the art that Appellants were in possession of the method of the invention as claimed. The written description rejection is reversed.

2. Claims 8-16 and 18-27 stand rejected under 35 U.S.C. § 102(b) as anticipated by Wold.

The Examiner finds that

> Wold disclose[s] methods of preparing agents comprising preparing an agent which includes a first non-peptidic moiety that binds to one cell surface receptor covalently linked to a

> second non-peptide moiety that binds to the other cell surface receptor, wherein the agent binds to both cell surface receptors (see page 618, lines 17-28; see pages 622 line 34 - page 640). …[T]he agents disclosed by Wold would bind to any two proteins, including cell surface receptors, or two endogenous protein mediators, which are in physical proximity, thereby effecting a biological function.

(Ans. 6.)

Appellants contend that "a skilled person in the art readily understands that the claim term "binds" is used in the art to refer to *noncovalent* associations (e.g., between an antibody and antigen or a receptor and a ligand). (Br. 19.)

Thus Appellants argue that:

> Wold does not teach methods that involve an agent that *binds* *n*on-covalently to two or more endogenous protein mediators. Instead, Wold teaches bifunctional reagents that *react with* and thereby form *covalent* bridges within or between proteins. . . . Based on the foregoing, Appellant has argued that the pending claims cannot be anticipated by Wold since it fails to teach an agent that *binds* to proteins.

(Br. 19.)

As we have concluded herein, we agree with Appellants' claim interpretation that the term "bind" in the claims would reasonably be interpreted as limited to non-covalent binding and would be understood to differ from the covalent bonding as described in Wold. In view of the above, we do not find that the Examiner has provided adequate evidence that Wold anticipates the pending claims. The anticipation rejection is reversed.

3. Claims 8-29 stand rejected under 35 U.S.C. § 102(b) as anticipated by Ji. The Examiner contends that Ji

> disclose[s] methods of preparing agents comprising preparing an agent which includes a first non-peptidic moiety that binds to one cell surface receptor covalently linked to a second non-peptide moiety that binds to the other cell surface receptor, wherein the agent binds to both cell surface receptors, including such agents as formaldehyde and gluteraldehyde.

(Ans. 6-7.)

The Examiner argues that "the agents disclosed by Ji would bind to any two proteins, including cell surface receptors, or two endogenous protein mediators, which are in physical proximity, thereby effecting a biological function." (Ans. 7.)

Appellants contend that

> Ji does not teach methods that involve an agent that *binds* to two or more endogenous protein mediators. Instead, Ji teaches bifunctional reagents that *react with* and thereby form *covalent* bridges within or between proteins. . . . Nowhere does Ji remedy the deficiencies of Wold by teaching methods for preparing an agent that *binds* to two or more endogenous protein mediators. For these reasons and those discussed above with respect to Wold,

(Br. 22.)

As we have concluded herein, we agree with Appellant's claim interpretation that the term bind in the claims would reasonably be interpreted as limited to non-covalent binding and would be understood to differ from the covalent bonding as described in Ji. In view of the above,

we do not find that the Examiner has provided adequate evidence that Ji anticipates the pending claims. The anticipation rejection is reversed.

SUMMARY

The rejection of claims 8-29 under 35 U.S.C. § 112, first paragraph as failing to comply with the written description requirement is reversed.

The rejection of claims 8-16 and 18-27 under 35 U.S.C. § 102(b) as anticipated by Wold is reversed.

The rejection of claims 8-29 under 35 U.S.C. § 102(b) as anticipated by Ji is reversed.

No time period for taking any subsequent action in connection with this appeal may be extended under 37 C.F.R. § 1.136(a).

REVERSED

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